REMARKS

Applicants appreciate the allowance of Claim 68.

Applicants have the following comments in support of this amendment and in response to the Office Action.

Claim Amendments – Reference to Disclosure

Independent Claims 1, 10 and 51 have been amended to be more explicitly directed to a preferred embodiment of the present application, i.e. radiosensitizer agents comprising an *aqueous solution* of 4,5,6,7-Tetrabromoerythrosin. Such amendment removes explicit reference to the presence or absence of a liposome in such radiosensitizer agents from the claim language.

Support for the presently claimed aqueous solutions is found throughout the specification of the present application, including for example the following passage:

> "Applicants have discovered a class of agents that fits this criteria and is preferably used in the present invention. These agents are referred to as halogenated xanthenes and are illustrated in Figure 1b, where the symbols X, Y, and Z represent various elements present at the designated positions, and the symbols R^1 and R^2 represent various functionalities present at the designated positions. Chemical and physical properties (such as the chemical constituents at positions X, Y, and Z and the functionalities R^1 and R^2, along with molecular weight) of representative halogenated xanthenes are summarized in attached Table 1. While many of the halogenated xanthenes are highly soluble in *aqueous solution*, in general all demonstrate a preference for selective partitioning into hydrophobic environments, such as within cell membranes." (p. 8, lines 5-14, emphasis added)

This passage makes it clear that the claimed halogenated xanthenes are highly soluble in aqueous solution, that such aqueous solutions are suitable for selective delivery to tissue, and accordingly that such aqueous solutions are suitable for use in the manufacture of the claimed radiosensitizer agents using certain halogenated xanthenes.

Accordingly, Applicants respectfully submit that this amendment does not add any new matter, and that the amendments to the claims are clearly supported by the application as filed. Therefore, it is requested that they be entered and allowed.

Novel Composition of Matter

Independent Claims 1, 10 and 51 are directed to radiosensitizer agents that contain a certain highly-halogenated halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin, which Applicants believe is not described in any prior art reference, and is definitely not described nor contemplated in the prior art of record.

Due to the relative complexity of synthesis of such compounds and other factors, such as stability considerations, Applicants believe that 4,5,6,7-Tetrabromoerythrosin is a new compound which represents a novel extension to the halogenated xanthene family. For example, Rose Bengal (which formerly comprised the most halogen-rich member of the halogenated xanthene family) has been known for over 100 years. Nonetheless, knowledge of its properties and those of the other previously known halogenated xanthenes (such as phloxine B, erythrosin, and eosin) has not led those skilled in the art to conceive, suggest, synthesize or investigate 4,5,6,7-Tetrabromoerythrosin.

Nor has anyone else conceived of pharmaceutical compositions consisting of halogenated xanthenes for radiosensitization prior to Applicants' work.

Accordingly, Applicants respectfully submit that 4,5,6,7-Tetrabromoerythrosin, and the various claimed compositions containing 4,5,6,7-Tetrabromoerythrosin, of the claims of the present application are novel over the prior art.

Applicants will now address each of the Examiner's rejections in the order in which they appear in the Office Action.

Claim Rejections – 35 USC §112

In the Office Action, the Examiner rejects Claims 1, 4, 10, 14, 15, 51, 55-57, 61, 65 and 66 under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. This rejection is respectfully traversed.

In support of this rejection, the Examiner states that "the specification does not appear to provide literal or adequate descriptive support for the recitation of 'said radiosensitizer agent does not include a liposome.'" As described supra, the rejected independent claims have been amended, removing the negative limitation excluding liposomes, and thereby rendering this rejection moot.[1]

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Statutory Double Patenting

A. USSN 09/799,785 in light of Windholz et al.

The Examiner provisionally rejects Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65 and 66 under 35 U.S.C. §101 for alleged double patenting over claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43 and 45-48

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[1] Applicants note that the amended claim language maintains exclusion of liposomes from the presently claimed radiosensitizer agents without requiring the objected negative limitation. Specifically, it is clear from the definition of a liposome that such aqueous solutions exclude liposomes from the claimed agent. For example, according to a standard medical dictionary (Stedman's Medical Dictionary, 27th Edition, Lippincott Williams & Wilkins, Philadelphia, 2000, p. 1022, attached), a liposome is defined as:

> "1. A spherical particle of liquid substance suspended in an aqueous medium within a tissue. 2. Any small, roughly spherical artificial vesicle consisting of a lipid bilayer enclosing some of the suspending medium."

Thus, the presently claimed radiosensitizer agents, comprising an aqueous solution of the halogenated xanthene 4,5,6,7-Tetrabromoerythrosin, cannot contain liposomes since if they did such agents would thereby comprise suspensions instead of solutions.

of copending U.S. application no. 09/799,785 in light of Windholz et al. This provisional rejection is also respectfully traversed.

Independent claims 1, 26, 42 and 46 of the '785 application are directed to certain *photodynamic* medicaments or pharmaceutical compositions, whereas the rejected claims of the present application are directed to radiosensitizer agents. Since the claimed photodynamic medicaments and pharmaceutical compositions of the '785 application require activation with *visible light*, whereas radiosensitizer agents require activation with *ionizing radiation*, these are two different inventions. While the two entities may contain common components (i.e., certain halogenated xanthenes), they are nonetheless distinct and separately patentable.

By way of example for such distinction, Applicants note that a transistor and diode each are substantially comprised of silicon, have metallic leads, and are electronic components. Nonetheless, these are distinctly different entities and have been the basis for numerous patentable inventions. A key basis for this distinction is in how the silicon is prepared and packaged for its ultimate use as either a transistor or a diode. Similarly, whereas the photodynamic medicaments and pharmaceutical compositions of the '785 application and the radiosensitizer agents of the present application are substantially comprised of certain halogenated xanthenes, the details of preparation and packaging for their respective ultimate use will differ, rendering their scopes non-coextensive. For instance, the photodynamic medicaments and pharmaceutical compositions of the '785 application will bear labeling indicating that to function they must be used (a) at a certain effective dosage (b) in conjunction with visible light (c) for certain types of medical treatment. In contrast, the radiosensitizer agents of the present application will bear labeling indicating that to function they must be used (a) at a different certain effective dosage (b) in conjunction with ionizing radiation (c) for certain other types of medical treatment.

Further, the present application is a divisional of the '787 application (now US 6,331,286), which was filed on December 21, 1998. Applicants' copending '785 application was filed on March 6, 2001 based on a provisional application filed March 24, 2000.[2]

Therefore, the claims of the '785 application, alone or taken together with Windholz, are not coextensive in scope with those of the present application.

Accordingly, Applicants respectfully request that this provisional rejection be withdrawn.

B. Priority over USSN 0/799,785

The Examiner also questions priority of Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65 and 66 relative to claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43 and 45-48 of copending U.S. application no. 09/799,785, and requests that Applicants state which entity is the prior inventor of the conflicting subject matter. This rejection is also respectfully traversed.

As explained above, the claims of these two applications are non-coextensive and non-conflicting.

Further, all four inventors of the present application are listed as inventors for the '785 application, along with Walter Fisher.

Nonetheless, the present application is a divisional of the '787 application, which was filed on December 21, 1998. Applicants' copending '785 application is a continuation-in-part of the '787 application (and other applications), and was filed on March 6, 2001.

Accordingly, Applicants are the inventor of the material of the present application.

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[2] The '785 application is a continuation-in-part of the '787 application (the parent of this application) and other applications. The specific subject matter of the pending claims herein is not believed to be disclosed in any of the earlier applications, other than the '787 parent application.

Obviousness Double Patenting

The Examiner provisionally rejects Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65 and 66 for alleged obviousness-type double patenting over claims 1, 4-6, 12-14, 29, 32-34, 39, 40 and 46-49 of copending U.S. application no. 09/817,448 in view of Heitz et al. (US 4,846,789). This provisional rejection is also respectfully traversed.

Applicants note that the present application is a divisional of application no. 09/216,787 (now US 6,331,286) which was filed on December 21, 1998. Hence, the present application can claim priority to the December 21, 1998 filing date, which is prior to the filing date of March 26, 2001 of the '448 application (or the provisional application filed April 6, 2000 for which the '448 application is based).

Further, Applicants' copending '448 application is also a continuation-in-part of the '787 application.

While Applicants traverse this rejection, in order to advance the prosecution of this application, Applicants are submitting herewith a terminal disclaimer and fee with regard to the '448 application. Accordingly, it is respectfully submitted that this rejection has been overcome, and it is requested that the rejection be withdrawn.

Claim Rejections – 35 USC §102 – Heitz

The Examiner rejects Claims 1, 10, 51, 52, 56, 57 and 66 under 35 U.S.C. §102(b) for alleged anticipation by Heitz et al. (US 4,846,789). This rejection is respectfully traversed.

First, as explained supra, the radiosensitizer agents of the claims of the present application are comprised of certain formulations of 4,5,6,7-Tetrabromoerythrosin, which is a *novel composition of matter* and a non-obvious extension of the halogenated xanthene class of molecules.

There is **no** disclosure or suggestion in Heitz of 4,5,6,7-Tetrabromoerythrosin. In fact, there is no disclosure or suggestion in Heitz on the subject of the possibility of such highly halogenated halogenated xanthenes, as evidenced by the passage cited by the Examiner:

> "The xanthene derivatives, and especially the *xanthene dyes having colour index numbers of 45000-45999*, are presently preferred in practicing the invention. The xanthene dyes are disclosed on Pages 4417-4430 of the aforementioned publication entitled Colour Index, and reference may be had thereto for numerous specific xanthene dyes. Additional xanthene dyes include those *prior art derivatives of xanthene* per se which absorb electromagnetic radiation having wave lengths falling within the ranges set out above. The derivatives of fluorescein (C.I. No. 45350) having one or more substituents in the 4, 5, 6, 7, 2', 4', 5' and 7' positions selected from the group consisting of F, Cl, Br, I, --NO.sub.2, --COOH and --OH are especially important. Specific examples of presently preferred xanthene dyes include erythrosin B (C.I. No. 45430), phloxin B (C.I. No. 45410), eosin yellowish (C.I. No. 45380), Rose Bengal (C.I. No. 45440) and rhodamine B (C.I. No. 45170)." (col. 4, lines 12-31, emphasis added)

The dyes having colour index number of 45000-45999 and the cited prior art derivatives of xanthene, do not include 4,5,6,7-Tetrabromoerythrosin nor is there any mention in the reference of this compound. Accordingly, Heitz does not anticipate or render obvious 4,5,6,7-Tetrabromoerythrosin.

Second, Heitz does not disclose or suggest the claimed radiosensitizer agents. In fact, Heitz is not in any way relevant to the present invention, and one skilled in the art would not consider this reference in designing a radiosensitizer agent for treatment of disease. Instead, Heitz is directed to pesticidal compositions and uses. This is clear from the following Summary of the Invention in Heitz:

> "The present invention utilizes the dyes described hereinafter and exposure to electromagnetic radiation to initiate one or more lethal photo-oxidative *reactions in certain internal parasites* of warm blooded animals. The parasites are endoparasitic helminths and/or pathogenic gastrointestinal protozoa having a life cycle which includes a life stage within the animals and a *life stage outside of the animals*. The parasites are *normally protected from exposure to*

> *natural electromagnetic radiation* having a wave length falling within the *visible spectrum* during at least most of the life stage within the animals, but they are *normally exposed to electromagnetic radiation* during at least a portion of the life stage *outside of the animals*
>
> "In practicing the method of the invention, *the internal parasites are caused to incorporate therein a photosensitizing amount of a dye.... Thereafter the parasites* having the dye incorporated therein *are exposed to electromagnetic radiation* of a wave length absorbed by the dye to thereby form cytotoxic oxygen and initiate at least one lethal oxidative reaction within the resulting photosensitized parasites. The parasites are preferably in the infective stage, thereby causing the life cycle to be broken. This markedly *reduces or prevents reinfection and the need for treating the animals with traditional anthelmintics*." (col. 1, 33-62, emphasis added)

This passage makes it clear that the disclosure in Heitz pertains to pesticidal use (i.e., *ex vivo* killing of intestinal parasites). In fact, Heitz does not treat disease in the animal at all but rather prevents transmission of pathogens from one infected animal to another animal (i.e., the pathogenic organisms are killed outside of the infected animal before they can be ingested and infect another animal). This is evidenced by the following passage from Heitz:

> "The aforementioned internal parasites ... should have a life cycle which includes a life stage within the host animal and a *life stage outside of the host animal*. The parasites are *protected from exposure to natural electromagnetic radiation having a wave length falling within the visible spectrum* during at least most, and preferably all or substantially all, of the life stage *within the host animal*. However, the parasites are normally *exposed to electromagnetic radiation*, which is usually *natural or artificial visible light*, during at least a portion of their life stage *outside of the host animal*." (col. 2, line 50-61, emphasis added)

Hence, the pathogens are killed by exposure to electromagnetic radiation during a period when they are *outside of the host animal*. This exposure occurs in the feces of the animal host upon exposure to light energy outside of the body, killing pathogenic organisms in excreted fecal pats and thereby preventing transmission to another host animal as explained in Heitz as follows:

> "As a general rule, the endoparasitic helminths usually reside in the gastrointestinal tract as adults and produce large numbers of eggs which are passed from the animal host in the feces... *The fecal pats are normally exposed to visible light*, and the *hatching eggs and larvae stages developing therefrom are likewise exposed to visible light*.... In the presence of visible light, substantially all of the *larve are killed before they are able to reinfect* the animal host." (col. 5, line 48 - col. 6, line 20, emphasis added)

Accordingly, the disclosure in Heitz does not therapeutically affect the animal to which the photosensitive dye is fed, but rather serves to break the chain of transmission of pathogens from one infected animal to another once the pathogens are exposed to light outside of the host animal's body. Therefore, the disclosure in Heitz is not directed nor does it disclose or suggest a radiosensitizer agent (i.e., a therapeutic agent for treatment of disease), as required in independent Claims 1, 10 and 51 of the present application.

Third, Heitz does not disclose or suggest radiosensitization using applied ionizing radiation, as required in independent Claims 1 (which requires application of ionizing radiation), 10 (which requires application of x-rays having an energy greater than 30 keV) and 51 (which requires application of ionizing radiation having an energy greater than or equal to 1 keV). Instead, Heitz contemplates use of optical energy, including visible light, near infrared light, and near to far ultraviolet light (see col. 3, lines 36-45 in Heitz). Such light has energy far below that recited in the independent claims of the present application and underlies the fundamental reason why the disclosure in Heitz requires exposure of pathogens to light energy outside of the body (such light cannot penetrate into the body), whereas Applicants' claimed invention allows delivery of activating energy (i.e., highly penetrating ionizing radiation) to any location within the body, thereby allowing disease to be treated in situ. In fact, Heitz makes no disclosure or suggestion of any interaction of

any agent with ionizing radiation, and therefore completely misses and effectively teaches away from the topic of radiosensitization.

Fourth, the compositions in Heitz are not suitable for intracorporeal use, as in the present application, since they are not sterile nor pyrogen free, as one of ordinary skill in the art would understand to be required of any radiosensitizer agent to be administered to the body. Instead, Heitz describes certain animal feed additives which of course are generally not sterile nor pyrogen free, as evidenced by the following passage from Heitz:

> "The dye may be administered to the animal in the form of an additive to its daily feed ration, in capsules, compressed pellets, boluses, salt blocks and the like. In the case of poultry, the dye may be incorporated within a synthetic grit...." (col. 5, lines 25-29)

Consumption of such feed additives leads to absorption of a portion of the photosensitizing dye contained therein by parasites in the gastrointestinal tract of the animal as explained below in Heitz:

> "When the host animal is fed the dye described herein, the dye is admixed with the food to be digested and passes through the gastrointestinal tract. The dye is in contact with the exposed skin of the immature larvae stages and adult stages residing in the gastrointestinal tract, and it is also present in the food consumed by the adult nematodes. As a result, the nematodes in the immature larvae stages and/or adult stage appear to ingest, assimilate, absorb or otherwise incorporate the dye into their tissues." (col. 5, line 62 - col. 6, line 3)

Thus, the compositions in Heitz pass through the digestive system of the host without uptake into its tissues and do not, therefore, comprise radiosensitizer agents suitable for treatment of disease.

Finally, with regard to the 4,5,6,7-Tetrabromoerythrosin halogenated xanthene as an imaging contrast agent in Claim 66, as described supra, this compound is a novel composition of matter, and hence such a composition as a contrast agent is novel and nonobvious.

Since Heitz does not disclose or suggest 4,5,6,7-Tetrabromoerythrosin, the compositions in Heitz are not suitable for use as radiosensitizers, and Heitz fails to teach or suggest the recited ionizing radiation energy levels, the fundamental properties, and mechanisms of Applicants' claimed radiosensitizer agents, Heitz cannot anticipate nor render obvious the claimed invention of the present application, nor is Heitz even relevant to the claimed invention. Hence, it is not a proper reference to reject the claims of the present application.

For at least the above-stated reasons, Heitz fails to disclose or suggest the radiosensitizer agents of the independent claims of the present application. Accordingly, the claims of the present application are patentable over the cited reference, and it is respectfully requested that this rejection be withdrawn.

Claim Rejections – 35 USC § 103(a) – Heitz in view of Williams

The Examiner rejects Claims 4, 15, 55, 61 and 65 under 35 U.S.C. §103(a) for allegedly being unpatentable over Heitz et al. (US 4,846,789) in view of Williams et al. (US 5,576,013). This rejection is also respectfully traversed.

As discussed supra, Heitz fails to disclose or suggest the existence the claimed highly halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin. Similarly, Williams fails to disclose or suggest the existence of the claimed highly halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin. Since neither Heitz nor Williams discloses or suggests the subject matter of independent Claims 1, 10 or 51, then rejected dependent Claims 4, 15, 55, 61 and 65 are also not disclosed or suggested by Heitz in view of Williams, and these rejected claims are patentable thereover.

Moreover, Williams describes a method of dye-mediated photocoagulation based on intense optical illumination of treated tissues that is fundamentally unrelated to the present invention. The

invention in Williams appears to be predicated on application of pulses of laser light to very small areas of tissue (i.e., 25-2000 microns in diameter), for example as described by the following passage:

> "The laser energy delivered to the target vessels per light burst in the present invention is within the range from about 1 Joule/cm^2 (J/cm^2) to about 4000 J/cm^2, preferably within the range from about 1-300 J/cm^2, and more preferably within the range from about 10 J/cm^2 to about 200 J/cm^2." (col. 4, lines 22-26)

Such methods are completely unrelated to the subject of the present application (i.e., radiosensitization) and would not motivate one of ordinary skill in the art to apply such teachings, alone or in conjunction with those of Heitz, to arrive at the subject of rejected Claims 4, 15, 55, 61 and 65.

Therefore, it is respectfully submitted that the claims are patentable over Heitz in view of Williams, and Applicants respectfully request that this rejection be withdrawn.

Conclusion

For at least the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this Amendment or new claims, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

Date: January 6, 2006

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Design: Dan Pfisterer

Database design by Lexi-Comp Inc., Hudson, OH
Printed in the United States of America by World Color, Inc.

Library of Congress Cataloging-in-Publication Data

Stedman, Thomas Lathrop, 1853-1938.
Stedman's medical dictionary.—27th ed.
p.; cm.
ISBN 0-683-40007-X (regular)—ISBN 0-683-40008-8 (deluxe)
1. Medicine—Dictionaries. I. Title: Medical dictionary. II. Title.
[DNLM: 1. Medicine—Dictionary—English. W 13 S812m 1999]
R121 .S8 1999
610'.3—dc21

99-056094

00 01 02 03 04 05
1 2 3 4 5

teinemia. Medical management of patients with coronary artery disease (myocardial infarction, angina pectoris, history of coronary artery bypass graft or coronary angioplasty) and other atherosclerotic disorders (peripheral arterial disease, abdominal aortic aneurysm, carotid artery disease) includes detection and correction of hypercholesterolemia and hyperlipoproteinemia. Reducing elevated LDL cholesterol diminishes the risk of coronary artery disease; besides halting the progression of atherosclerosis, it may even shrink established atherosclerotic lesions. Of persons with elevated LDL cholesterol, 75% can achieve normal levels with diet, weight reduction, and exercise; the remainder need drug treatment. Factors besides familial hyperlipoproteinemias that can elevate LDL cholesterol include diabetes mellitus, hypothyroidism, nephrotic syndrome, obstructive liver disease, and drugs (progestogens, anabolic steroids, corticosteroids, thiazide diuretics). Dietary saturated fat raises LDL cholesterol more than any other dietary component, cholesterol itself not excepted.

l. (a), a l. consisting of an LDL particle to which a large glycoprotein, apolipoprotein (a), is covalently bonded. Elevation of the concentration in serum has been identified as a risk factor for coronary artery disease.

Elevation of plasma lipoprotein (a) above 30 mg/dL is a strong independent risk factor for coronary artery disease and possibly for stroke. A unique feature of lipoprotein (a) is the structural similarity of its nonlipid moiety, apolipoprotein (a), to plasminogen. This similarity allows it to bind to endothelium and to proteins of cellular membranes. It inhibits fibrinolysis by competing for plasminogen binding sites and also favors lipid deposition and stimulates smooth muscle cell proliferation. Niacin and estrogen lower Lp(a), but HMG-CoA reductase inhibitors, fibrates, and bile acid sequestrants do not.

α_1-l., A lipoprotein fraction of relatively low molecular weight, high density, rich in phospholipids, and found in the α_1-globulin fraction of human plasma.

β_1-l., A lipoprotein fraction of relatively high molecular weight, low density, rich in cholesterol, and found in the β-globulin fraction of human plasma.

intermediate density l. (IDL), class of l.'s formed in degradation of very low density l.'s; about half are cleared quickly from the plasma into the liver by receptor-mediated endocytosis; the other half are degraded into low density lipoproteins.

l. Lp(a), a l. composed of an LDL particle combined with an additional protein, Lp(a) specific protein; elevated levels have been identified as a risk factor for coronary artery disease; elevations may be treated with niacin.

malondialdehyde-modified low-density l., lDL molecule with aldehyde-substituted lysine residue(s) in the apoprotein moiety, resulting from oxidative reaction accompanying prostaglandin synthesis and platelet aggregation.

l.-X, An abnormal low-density lipoprotein found in patients with obstructive jaundice.

lip·o·pro·tein li·pase. An enzyme that hydrolyzes one fatty acid from a triacylglycerol; its activity is enhanced by heparin and inactivated by heparinase. It is activated by apolipoprotein C-II; a deficiency of l. l. is associated with familial hyperlipoproteinemia type I. SEE ALSO familial lipoprotein lipase *inhibitor*, clearing *factors*, under *factor*. SYN diacylglycerol lipase, diglyceride lipase.

lip·o·sar·co·ma (lip'ō-sar-kō'mă). A malignant neoplasm of adults that occurs especially in the retroperitoneal tissues and the thigh, usually deep in the intermuscular or periarticular planes; histologically, l. is a large tumor that may be composed of well-differentiated fat cells or may be dedifferentiated, either myxoid, round-celled, or pleomorphic, usually in association with a rich network of capillaries; recurrences are common, and dedifferentiated l. metastasizes to the lungs or serosal surfaces. [lipo- + *sarx*, flesh, + *-oma*, tumor]

li·po·sis (li-pō'sis). **1.** SYN adiposis. **2.** Fatty infiltration, neutral fats being present in the cells. SEE ALSO lipolipoidosis. [lipo- + G. *-osis*, condition]

li·pos·i·tol (lip-os'i-tol). SYN inositol.

lip·o·sol·u·ble (lip-ō-sol'ū-bl). Fat-soluble.

lip·o·some (lip'ō-sōm). **1.** A spherical particle of lipid substance suspended in an aqueous medium within a tissue. **2.** Any small, roughly spherical artificial vesicle consisting of a lipid bilayer enclosing some of the suspending medium. [lipo- + G. *sōma*, body]

lip·o·suc·tion (lip'ō-sŭk-shun). Method of removing unwanted subcutaneous fat using percutaneously placed suction tubes.

tumescent l., l. performed after subcutaneous infusion of lidocaine solution and the use of microcannulae.

wet-technique l., l. performed after subcutaneous infusion of dilute epinephrine solution.

lip·o·suc·tion·ing (lip'ō-sŭk'shŭn-ing). Removal of fat by high vacuum pressure; used in body contouring.

lip·o·thi·am·ide py·ro·phos·phate (lip-ō-thī'am-īd). Name once given to the coenzymes of the multienzyme complex catalyzing the formation of acetyl-CoA from pyruvate and involving lipoamide and thiamin pyrophosphate, on the assumption that they were a single compound. SEE lipoic acid.

lip·o·tro·phic (lip-ō-trof'ik). Relating to lipotrophy.

li·pot·ro·phy (li-pot'rō-fē). An increase of fat in the body. [lipo- + G. *trophē*, nourishment]

lip·o·tro·pic (lip-ō-trop'ik). **1.** Pertaining to substances preventing or correcting excessive fat deposits in liver such as occurs in choline deficiency. **2.** Relating to lipotropy.

lip·o·tro·pin (li-pō-trō'pin). A pituitary hormone mobilizing fat from adipose tissue. β-L. is a single-chain peptide of 91 amino acyl residues that contains the sequences of endorphins, metenkephalin, and β-melanotropin; γ-l. is shorter and is identical in sequence to the N-terminal 58 residues of β-lipotropin; both contain sequences common to ACTH and β-melanotropin. SYN lipid-mobilizing hormone, lipotropic hormone, lipotropic pituitary hormone.

plasma lipoproteins

chylomicrons	<0.95	90–1000	A-1, A-2, B-48, C-2, C-3, E	1–2	88	4
very-low-density lipoproteins (VLDL)	0.95–1.006	30–90	B-100, C-1, C-2, C-3, E	7–10	56	23
intermediate-density lipoproteins (IDL)	1.006–1.019	25–30	B-100	11	43	29
low-density lipoproteins (LDL)	1.019–1.063	20–25	B-100	21	58	13
high-density lipoproteins (HDL)						
HDL_2	1.063–1.125	10–20	A-1, A-2, A-4, C-1, C-2, C-3, D	33	41	16
HDL_3	1.125–1.210	7.5–10		57	35	13